



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,164	11/09/2006	Enrico Colli	62138US(49949)	6611

21874 7590 02/07/2008
EDWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER

QAZI, SABIHA NAIM

ART UNIT	PAPER NUMBER
----------	--------------

1612

MAIL DATE	DELIVERY MODE
-----------	---------------

02/07/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.		Applicant(s)	
	10/573,164		COLLI, ENRICO	
	Examiner		Art Unit	
	Sabiha Qazi		1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 August 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-4 and 7-22 is/are pending in the application.
- 4a) Of the above claim(s) 7 and 8 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-4 and 9-19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 7 and 8 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Non-Final Office Action

Claims 2-4, 7-22 are pending. No claim is allowed at this time. Amendments are entered. Claims 2-4 and 9-19 are examined; others are withdrawn from consideration as non-elected invention.

Summary of the Office Action Friday, August 31 dated 8/31/2007

1. Information Disclosure Statement
2. Copending Applications
3. Specification
4. 35 USC § 112 --- First Paragraph written Description Rejection
5. 35 USC § 103(a) Obviousness Rejection – First Rejection
6. 35 USC § 103(a) Obviousness Rejection – Second Rejection
7. Response to Remarks
8. Communication

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Copending Applications

Applicants must bring to the attention of the examiner, or other Office official involved with the examination of a particular application, information within their knowledge as to other copending United States applications, which are "material to patentability" of the application in question. MPEP 2001.06(b). See *Dayco Products Inc. v. Total Containment Inc.*, 66 USPQ2d 1801 (CA FC 2003).

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112—Written Description Rejection

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-4 and 9-22 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Following reasons apply.

There is no teaching or guidance how “prevention” and “treatment” of bladder dysfunction by such a large number of compounds would be treated successfully.

It appears that Applicant s have no possession of claimed subject matter at the time the invention was filed.. Applicant is kindly requested to show that at the time of invention Applicants were in possession of the claimed invention.

Art Unit: 1612

The written description requirement prevents applications from using the amendment process to update the disclosure in their disclosures (claims or specification) during the pendency before the patent office. Otherwise applicants could add new matter to their disclosures and date them back to their original filing date, thus defeating an accurate accounting of the priority of the invention. See 35 USC 132. The function of description requirement is to ensure that the inventor had possession, as of filing date of the application relied on, the specific subject matter claimed by him.

See *Genetech*, 108 F 3d 1361, 1365 (Fed. Cir. at 1366, 78, 1999).

The test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to one skilled in the art that the inventor had the possession at the time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claimed language. See *In re Kaslow*, 707 F 2d 1366, 1375 (Fed. Cir. 1983).

See MPEP 2163.06.

Double Patenting Rejection

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible

Art Unit: 1612

harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-2 and 9-19 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 8, 9, 11, 12, 15, 23, 24, 31 and 32 of Application No. 10/903,211 (recently allowed). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims of “211 are drawn to a

Art Unit: 1612

method for treating benign prostatic hyperplasia in a Patient in need of such treatment comprising administering to said patient a therapeutically effective amount of 1 -alpha-fluoro-25-hydroxy-16,23E-diene-26,27-bishomo-20-epi- cholecalciferol or a pharmaceutically acceptable salt or ester thereof. Claims of the present invention are drawn to a method of prevention or treatment of bladder dysfunction in a patient by administering to a patient in need thereof an effective amount of vitamin D compound thereby to prevent or treat bladder dysfunction in said patient.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 2 and 3 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention: Following reasons apply: Claim 3 is drawn to a method according to claim 2 which further comprises the **step of obtaining or synthesizing** the Vitamin D compound. There are no steps for synthesizing or method for obtaining vitamin D compounds. Claims are open ended.

Claim Rejections - 35 USC § 103—1st Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

Art Unit: 1612

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-4 and 9-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over BATCHO et al. United States Patent No. 5,939, 408, BISHOP et al. WO 98/29123 and BISHOP et al. (US Patent 6,566,353). These references teach vitamin D compounds useful for the treating benign prostatic hyperplasia (BPH), which embraces Applicant's claimed invention.

BATCHO teaches 1 α --flouro-25-hydroxy-16, 23E-diene-26, 27-bishomo-20-epi-cholecalciferol. See the entire document especially summary of invention in column 1 where R represents F, R₂ represents alkyl and X represents =CH₂, lines 55-65 in column 2, **example 38** (col. 34) and claim 26 which is drawn to a method for treating neoplastic disease. These compounds induce cell differentiation and inhibition of proliferation in various cancer cell lines. Various other uses are disclosed.

BISHOP WO '123 teaches method and composition of treating prostatic disease using active vitamin D compounds. The invention provides a method of treating prostatic disease conditions such as those characterized by hyperproliferative cell growth and/or abnormal cell differentiation, e.g. prostate cancer and prostate hyperplasia. See the entire document especially,

Art Unit: 1612

lines 1-10 on page 5. Furthermore, reference teaches addition of active agents such as 5 α -reductase enzyme inhibitor such as finasteride, flutamide etc. See lines 26-31 on page 13.

BISHOP US '353 teaches a method of treating hypercalcemia associated with malignant or neoplastic cells, comprising the cells with an effective amount of a vitamin D compound having a hydrocarbon moiety at C-24 position, where the cells are cancers of the bladder (see claim 1 and 2). See the entire document especially lines 52-67 in column 2, lines 1-65 in column 3, examples and claims

Instant claims are taught by all the references cited above.

It would have been obvious to one skilled in the art at the time of invention was made to use the 1 α --fluoro-25-hydroxy-16, 23E-diene-26, 27-bishomo-20-epi-cholecalciferol for treating prostate hyperplasia because BISHOP references teaches method of treating prostate hyperplasia by vitamin D compounds. The motivation to select this particular compound R0-26-9228 is because one would expect vitamin D compounds to inhibit prostate hyperplasia because BISHOP teaches the same use. The combination of various active agents is also taught by the prior art such as 5 α -reductase enzyme inhibitor, finasteride, flutamide. BISHOP further teaches a method of treating hypercalcemia associated with malignant or neoplastic cells, comprising the cells with an effective amount of a vitamin D compound having a hydrocarbon moiety at C-24 position, where the cells are cancers of the bladder. Since instant claims are drawn to "bladder dysfunction" it includes every disease which are caused by bladder dysfunction.

Art Unit: 1612

The invention as presently claimed appears to be a routine experimentation of the teachings of prior art at the time of invention. See KSR Supreme Court of United States Decision (Decided April 30, 2007, KSR INTERNATIONAL CO. v. TELEFLEX INC. et al. No. 04-1350) where it states that (1) "However, the issue is not whether a person skilled in the art had the motivation to combine the electronic control with an adjustable pedal assembly, but whether a person skilled in the art had the motivation to attach the electronic control to the support bracket of pedal assembly". (2) "the results of ordinary innovation are not the subject of exclusive rights under the patent laws". In the present case the method as claimed would have been obvious to one skilled in the art at the time the invention was made.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a)¹.

Claim Rejections - 35 USC § 103—2nd Rejection

Claims 2-4 and 9-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over BATCHO et al. United States Patent No. 5,939, 408, in view of CRESCIOLI et al. (J. of Clinical Endocrinology & Metabolism). These references teach vitamin D compounds useful for the treating benign prostatic hyperplasia (BPH), which embraces Applicant's claimed invention.

¹ Examiner notes, that SERIO ET AL. FR 97/A/000269 teaches vitamin D compound RO 23-7553 which is 1, 25-dihydroxy-16, 23-yne vitamin D3 for the treatment of BPH, see last two paragraphs on page 7, claims especially claims 1 and 7, Fig. 1 and 2.

Art Unit: 1612

BATCHO teaches 1 α --flouro-25-hydroxy-16, 23E-diene-26, 27-bishomo-20-epi-calciferol. See the entire document especially summary of invention in column 1 where R represents F, R₂ represents alkyl and X represents =CH₂, lines 55-65 in column 2, **example 38** (col. 34) and claim 26 which is drawn to a method for treating neoplastic disease. These compounds induce cell differentiation and inhibition of proliferation in various cancer cell lines. Various other uses are disclosed.

BATCHO does not teach specifically the treatment of prostate hyperplasia (it teaches the treatment of neoplastic disease by the same compound as presently claimed. (See claim 26 and example 38 in col. 34).

CRESCIOLI et al. teaches 1 α --25-dihydroxy-16, 23E-diene-D3 (analog V). The reference discloses the effect of vitamin D and its analog (V) on basal and KGF-induced proliferation and apoptosis in BPH cells. See results and fig. 2 on page 2579.

Instant claims differ from the reference in claiming method of prevention and/or treatment using specific compound 1 α --flouro-25-hydroxy-16, 23E-diene-26, 27-bishomo-20-epi-cholecalciferol.

It would have been obvious to one skilled in the art at the time of invention was made to use the 1 α --flouro-25-hydroxy-16, 23E-diene-26, 27-bishomo-20-epi-calciferol for treating prostate hyperplasia because BATCHO teaches 1 α --flouro-25-hydroxy-16, 23E-diene-26, 27-bishomo-20-epi-calciferol as presently for the treatment of neoplastic disease and CRESCIOLI teaches the non hypercalcemic analogue of vitamin D analog decreases growth factor induced human BPH cell proliferation and survival. The motivation to select compound R0-26-9228 as

Art Unit: 1612

claimed because one would expect vitamin D compounds to inhibit prostate hyperplasia because CRESCIOLI teaches the same use.

Furthermore, the combination of various active agents is also taught by the prior art such as 5 α -reductase enzyme inhibitor, finasteride, flutamide.

The invention as presently claimed appears to be a routine experimentation of the teachings of prior art at the time of invention. A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill might reasonably infer from the teachings. *In re opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA 1976). A reference is not limited to working examples. *In re Fracalossi* 215 USPQ 569 (CCPA 1982).

Accordingly, the burden of proof is upon applicants to show that instantly claimed subject matter is different and unobvious over those taught by prior art. See *In re Brown*, 173 USPQ 685, 688; *In re Best*, 195 USPQ 430 and *In re Marosi*, 218 USPQ 289, 293.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a)².

Response to Remarks

Election of group I, claims 2-4 and 9-22 is hereby acknowledged. Applicants arguments were fully considered but are not found persuasive therefore restriction is maintained for the same reasons as set forth in the previous office action.

Art Unit: 1612

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi, Ph.D. whose telephone number is 571-272-0622. The examiner can normally be reached on any business day.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter, Ph.D. can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



SABIHA QAZI, PH.D
PRIMARY EXAMINER

² Examiner notes, that SERIO ET AL. FR 97/A/000269 teaches vitamin D compound RO 23-7553 which is 1, 25-dihydroxy-16, 23-yne vitamin D3 for the treatment of BPH, see last two paragraphs on page 7, claims especially claims 1 and 7, Fig. 1 and 2.